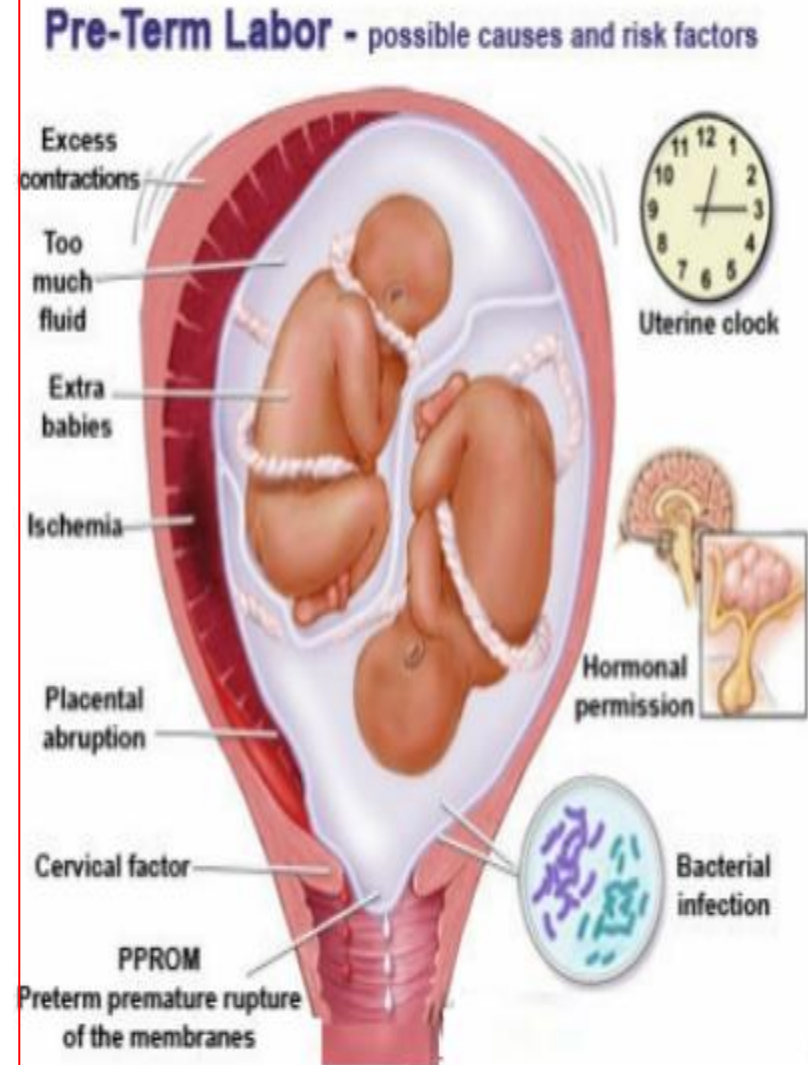


Tocolytics and Oxytocics

Lecture-1-
Reproductive Block
Ahlam Sultan

Tocolytics

- **Pre-term birth, or labor that occurs before the 37 week** of pregnancy is one of the main clinical problems in obstetrical practice
- The incidence of Pre-term birth may differ in different regions, the rate varying worldwide in the range between **5–11%**
- It is responsible for 85% of neonatal illnesses and death
- Tocolytics are used to delay labor when there are premature uterine contractions



Tocolytics

- **Tocolytics** or uterine relaxants reduce uterine motility and contraction

Goal:

- ✓ Allow additional time for fetal maturation
- ✓ Initiate glucocorticoid therapy for fetus lung maturation
- ✓ Transfer the women in labour to proper facilities
- They are likely to succeed only when the cervical dilatation $< 4\text{cm}$
- Tocolytics rarely delays delivery beyond **24–48 hours**



Corticosteroid therapy

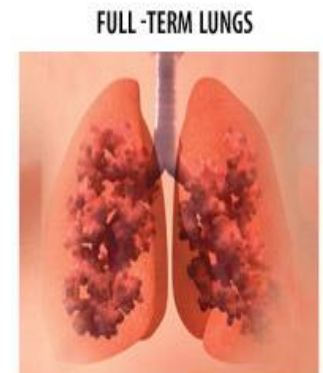
- **Clients at risk for preterm delivery should receive corticosteroid therapy with:**
 - ✓ Betamethasone
 - ✓ Dexamethasone
- **Goals:**
 - ✓ Accelerates **lung maturation** and **lung development** in the fetus in uterus
 - ✓ Decreasing the incidence and severity of **respiratory distress syndrome**
 - ✓ Increase **survivor of preterm infants**

Doses:

- **Betamethasone** is 12mg IM q24 h for 2 dose
- **Dexamthasone** is 6 mg IM q12h for 4 doses



32 WEEKS GESTATIONAL AGE



40 WEEKS GESTATIONAL AGE

Tocolytics

Class	Drugs
β_2-adrenergic agonist	✓ Salbutamol ✓ Terbutaline ✓ Ritodrine
Calcium Channel blockers (CCBs)	✓ Nifedipine ✓ Nicardipine
Cyclooxygenase inhibitors (Prostaglandin inhibitors)	✓ Aspirin ✓ Indomethacin
Oxytocin antagonists	✓ Atosiban
Miscellaneous	✓ Magnesium sulfate



Tocolytics

Uses:

1. To delay premature labor
2. In threatened abortion to inhibit uterine contractions
3. Dysmenorrhoea



Tocolytics

Contraindication:

1. Fetus is > 34 weeks gestation
2. Fetus has intrauterine growth restriction or placental insufficiency
3. Lethal congenital or chromosomal abnormalities
4. Cervical dilation is > 4 cm
5. intrauterine infection is present
6. Mother has severe pregnancy-induced hypertension, eclampsia/preeclampsia, active vaginal bleeding, placental abruption, a cardiac disease, or another condition which indicates that the pregnancy should not continue
7. Other cause of fetal distress or fetal death

β_2 -adrenergic agonists

E.g., Terbutaline , Salbutamol and Ritodrine

- ✓ β_2 -adrenergic agonists are among the most frequently used tocolytics
- ✓ Stimulating the **β_2 receptors** on uterine smooth muscle are known to produce smooth muscle cell relaxation
- ✓ The frequency and intensity of **uterine contractions decrease as the muscle relaxes**

Side effects:

- Maternal:

- ✓ Tachycardia
- ✓ Hyperglycemia
- ✓ Pulmonary oedema
- ✓ Hypokalemia

- Foetal:

- ✓ Tachycardia
- ✓ Hyperinsulinemia/hypoglycemia

β ₂-adrenergic agonists

E.g., Terbutaline , Salbutamol and Ritodrine

MOA:

- ✓ Bind to β -adrenoceptors , activate enzyme Adenylate cyclase , increase in the level of cAMP reducing intracellular calcium level



β 2-adrenergic agonists

E.g., Terbutaline , Salbutamol and Ritodrine

- Salbutamol given as i.v. Infusions
- Ritodrine by i.v. Infusion, i.m. Or oral
- Terbutaline by i.v. Or oral
- Continued for 12 hours after the contractions cease

Contraindicated:

1. Diabetic
2. Cardiac disease
3. Hypertension or hyperthyroidism
4. Pregnant women taken one of the following medication:
 - ✓ Beta blocker
 - ✓ Digoxin

Magnesium Sulfate

- ✓ Act as **competitive inhibitor of calcium ions at motor endplate/ cell membrane reducing calcium influx**
- ✓ It has a direct depressant effects on uterine muscle contractility
- ✓ **Relaxes** the smooth muscle of the uterus
- ✓ **Safer** to be used compared to beta-sympathomimetics but high doses can cause significant CNS and respiratory depression
- ✓ Used as alternative when adrenergic agonist are contraindicated
- ✓ Antidote: **calcium gluconate**



The colorful safety label is applied to the 4 gram magnesium bag by the pharmacy inventory technician immediately upon receipt.

Magnesium Sulfate

- Given by i.v. infusion, loading dose: 4-6 gm. i.v. over 15 to 20 minutes
- Infusion: 1-2 gm/ hour, continued for 12 hours after cessation of contractions

Other uses:

- 1- Hypomagnesimia
- 2- Eclampsia in pregnant women

Contraindicated:

1. Renal failure
2. Myasthenia gravis
3. Cardiac disease

Side effects:

• Maternal:

- ✓ Visual blurring
- ✓ Headache
- ✓ Flushing
- ✓ Hypotension

• Foetal:

- ✓ Hypotonia
- ✓ Respiratory depression

Calcium Channel Blockers (CCBs)

- E.g., **Nifedipine** and **Nicardipine**
- ✓ Calcium channel blockers (CCBs) are among the frequently used tocolytics
- ✓ They are **constantly gaining in importance**, and increasingly more significant than traditional tocolytics such as beta-adrenergic receptor blockers or magnesium sulphate

Side effects:

- Maternal:

- ✓ Headache
- ✓ Tachycardia
- ✓ Hypotension
- ✓ Flushing
- ✓ Peripheral edema

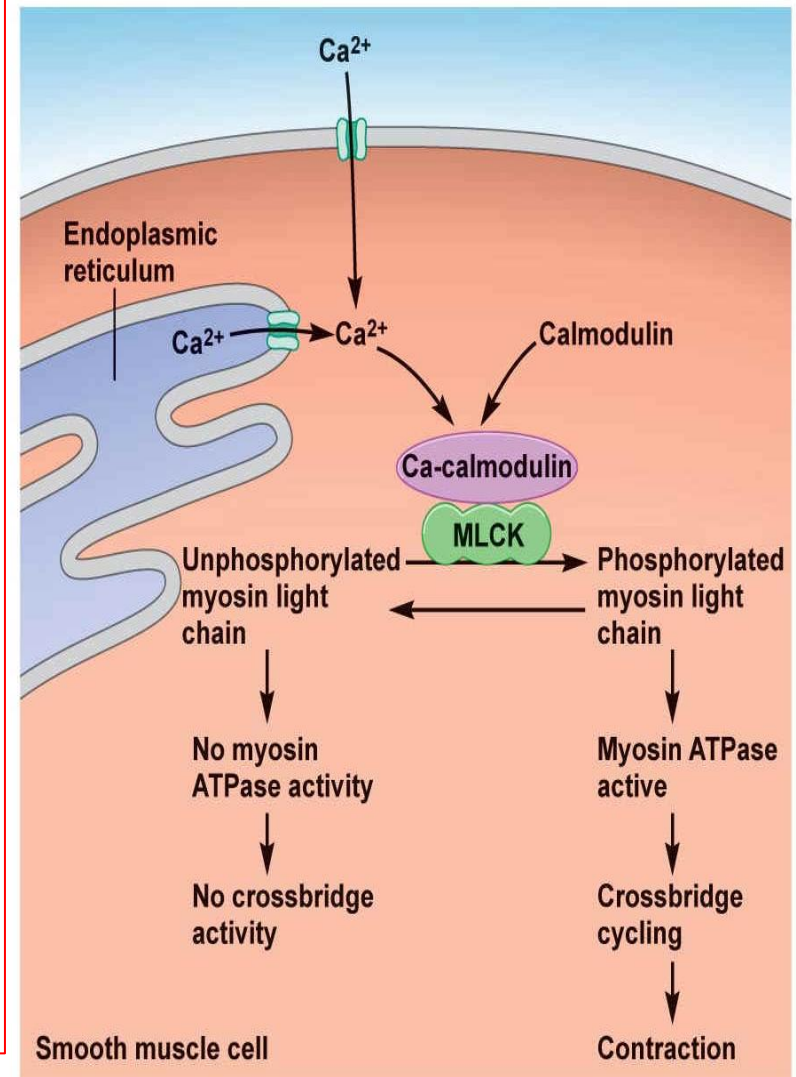
- Foetal:

- ✓ Hypoxia (reduce placental perfusion)

Calcium Channel Blockers (CCBs)

MOA:

- They **block the influx of Ca^{2+} ions**, thereby reducing the intracellular calcium and reduce the tone and myometrium contraction
- ✓ Uterine contractile activity is regulated by the increase in intracellular Ca^{2+} concentration in the myometrial cells
- ✓ Voltage-gated Ca^{2+} channels mediate the Ca^{2+} influx in response to membrane depolarization and regulate intracellular processes such as contraction



Calcium Channel Blockers (CCBs)

- Oral nifedipine 10 mg every 20-30 minutes, till uterine contractions subside, followed by 10 mg every 6 hourly
- **Contraindication:**
 1. CHF
 2. Hypotension
 3. Sever aortic stenosis



Oxytocin antagonists

E.g., Atosiban

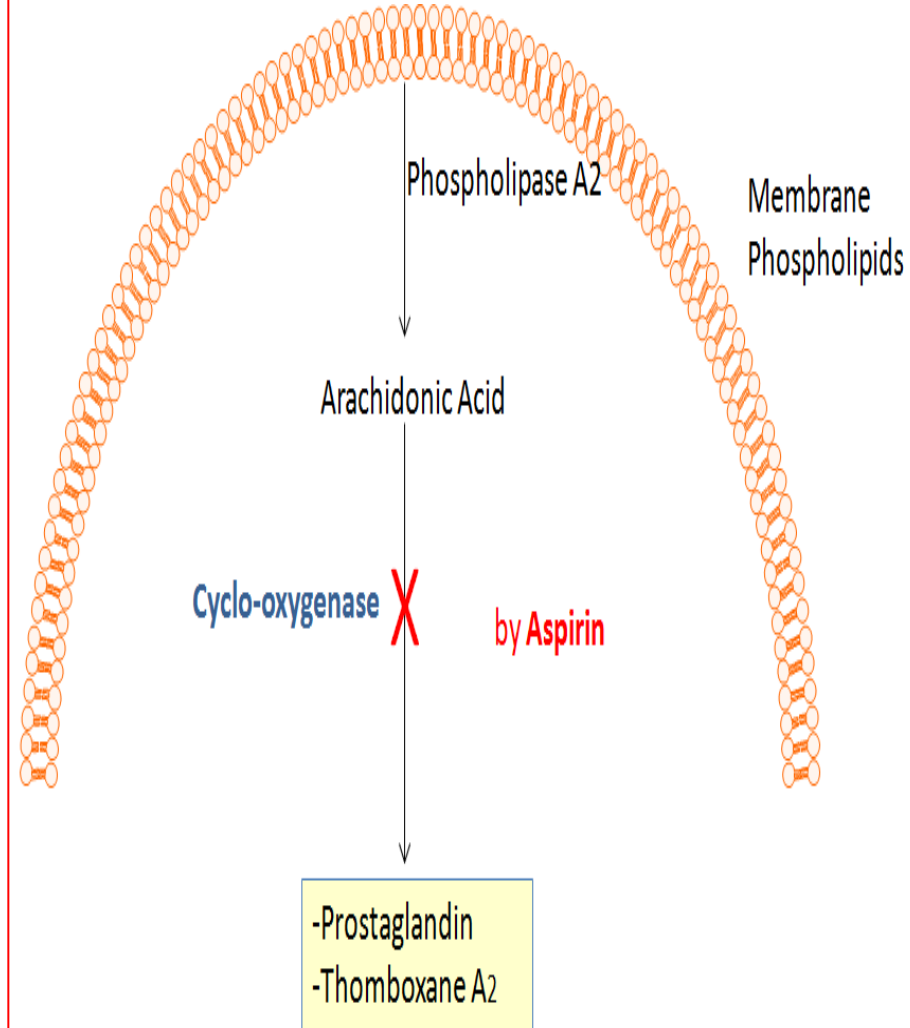
- Atosiban is a peptide analogue of oxytocin, acts as an **antagonist at oxytocin receptors**
- Has been licensed for use in pre-term labour
- It is **preferable** to beta2 agonist because it has fewer side effects

Side effects:

- Maternal:
 - ✓ Tachycardia
 - ✓ Hypotension
 - ✓ Headache
 - ✓ Hot flushing
 - ✓ Hyperglycemia

Aspirin

- Aspirin **inhibit cyclooxygenase by irreversible acetylation**
Thus inhibits prostaglandin synthesis
- **Prostaglandins** are important mediators of uterine activity
- Aspirin is not preferred as tocolytic because of the risk of ductus arteriosus



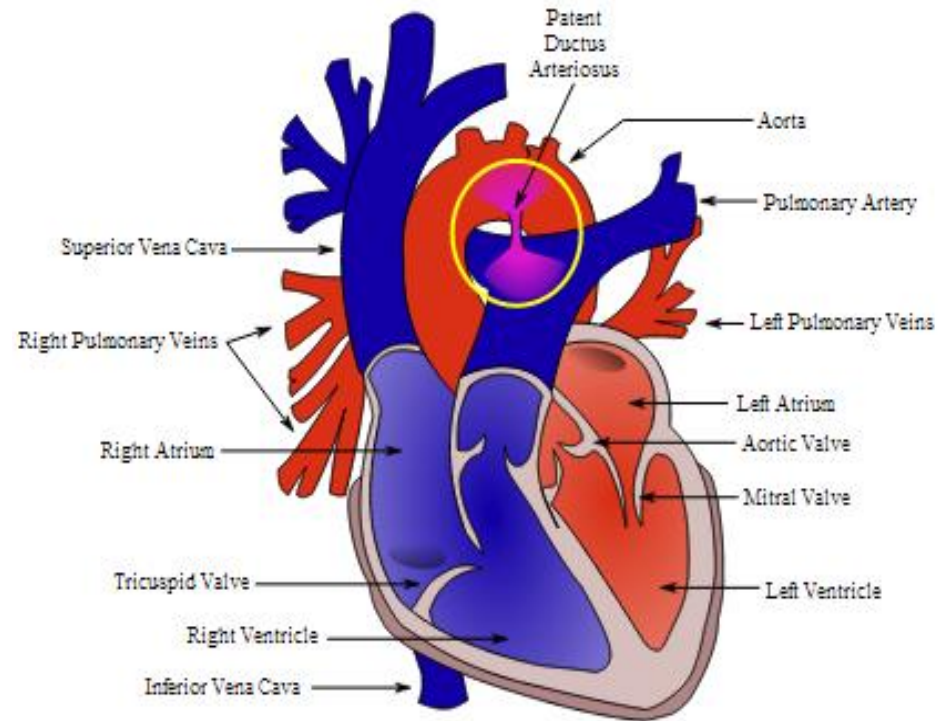
Aspirin

Side effects:

- Maternal:
 - ✓ GI Bleeding
 - ✓ Acute renal failure
- Foetal:
 - ✓ Premature closure of Ductus arteriosus

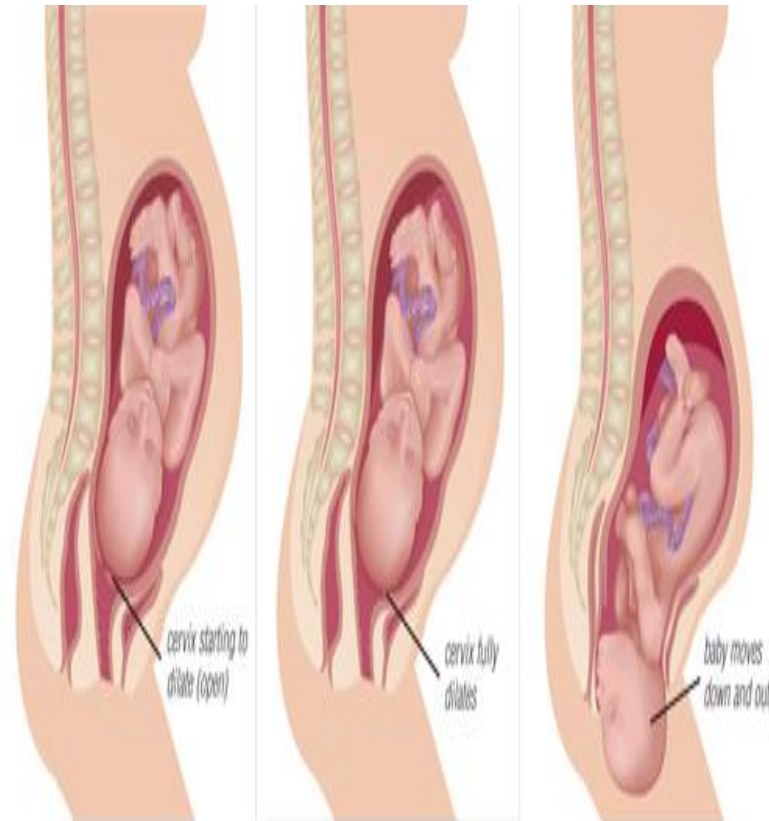
Contraindications:

1. Thrombocytopenia
2. Bronchial asthma
3. Renal disease



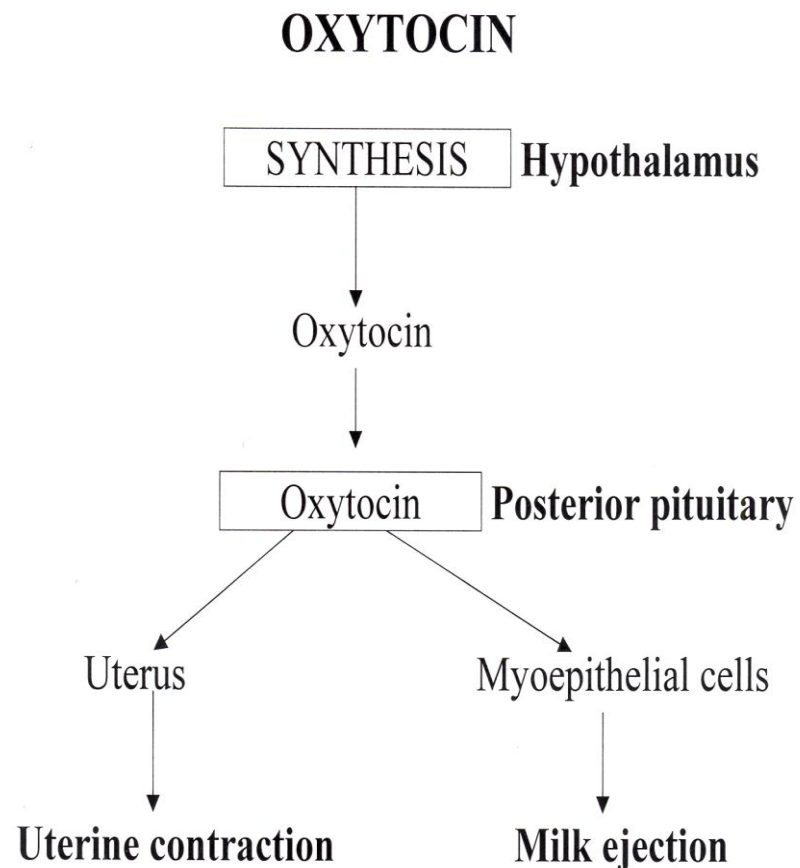
Oxytocic

- Oxytocic are also called **uterine stimulant**
- Drugs that enhance uterine contractility by stimulating the smooth muscle of the uterus, e.g:
 - ✓ Oxytocin
 - ✓ Prostaglandins: PGE₂ or PGF₂ α
 - ✓ Ergometrine



Oxytocin

- Hormone secreted by the posterior pituitary along with ADH (vasopressin)
- It is synthesized in the hypothalamus and stored in the neurohypophysis
- It is released by stimuli such as suckling, coitus and parturition



Oxytocin

MOA:

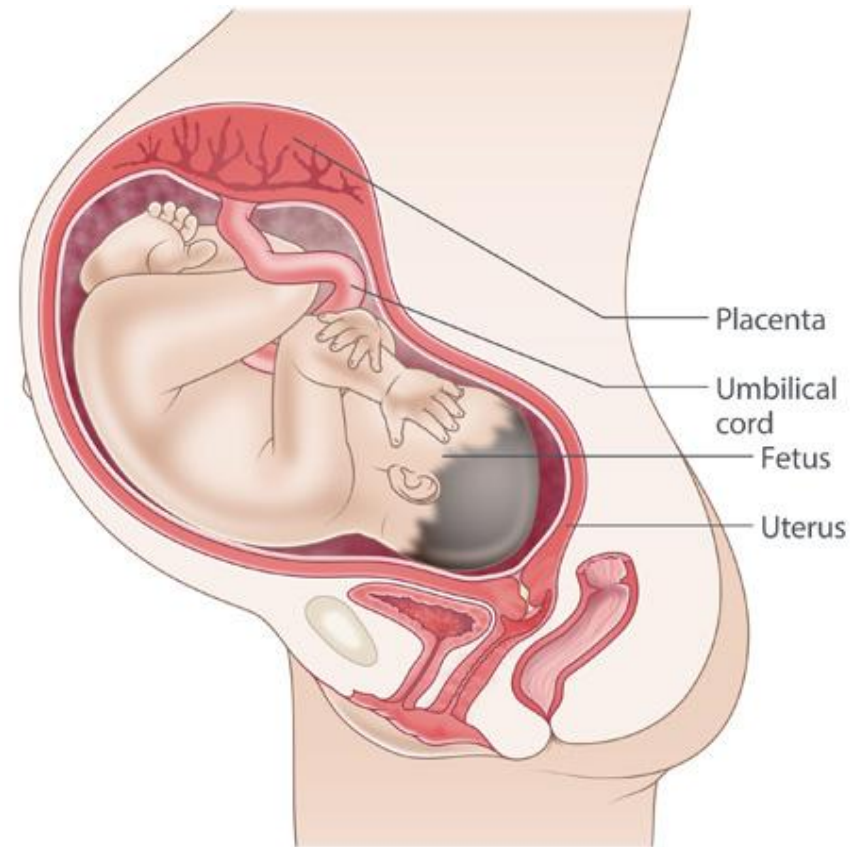
- ✓ Promote uterine contractions by **increasing intracellular concentrations of calcium** in uterine myometrial tissue
- ✓ Nasal spray promote milk ejection by causing **contraction of the smooth muscle fiber surrounding the breast alveoli and ducts**



Oxytocin

Uses:

- 1- Induce labor contractions
- 2- Treat uterine atony
- 3- Postpartum hemorrhage (PPH)
- 4- Stimulate milk letdown (nasal spray)
- 5-Abortion



Oxytocin

Contraindications:

- Unfavorable fetal positions
- Fetal distress
- Hypertonic or hyperactive uterus
- Mechanical obstruction to delivery

Side effects:

Maternal:

- ✓ Water intoxication (ADH)
- ✓ Excess uterine contractions
- ✓ Uterine rupture

Foetal:

- ✓ Foetus distress
- ✓ Foetal hypoxia (uterine hyperstimulation)

Ergometrine

- Ergometrine and its derivative methylergometrine are used as uterine stimulants
- Ergot has been used by midwives to quicken labor since centuries

Uses: (It is usually used in combination with oxytocin):

- Control and prevent postpartum hemorrhage
- Prevent uterine atony

Side effects:

- Nausea
- Vomiting
- Hypertension (rare)

Ergometrine

Actions:

- Ergometrine is a powerful uterine stimulant
- The force and frequency of uterine contraction are enhanced
- There is no relaxation in between contractions
- Full-term uterus is more sensitive to the action of ergometrine
- Ergometrine also cause some VC which helps to reduce bleeding from the uterus in postpartal state



Prostaglandins

- Prostaglandins synthesized by the uterus play a significant role in menstruation as well as parturition
- PGE₂ or PGF_{2α} **stimulate the contraction of both pregnant and nonpregnant uterus** though sensitivity is higher during pregnancy
- They also soften the cervix and hasten cervical dilatation

- **Dinoprostone (PGE₂):**
 - ✓ Intravaginal
- **Carboprost (PGF_{2α}):**
 - ✓ Deep IM
- **Misoprostol (PGE₁):**
 - ✓ Intravaginal, orally

Prostaglandins

Uses:

1. Induce Abortion
2. Postpartum hemorrhage
3. Cervical priming gels are used intravaginally to soften the cervix and for cervical reopening prior to induction of labor
4. Induction of labor

